



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/074,744	02/13/2002	Malla Padidam	A01183	1483

7590

03/24/2004

RheoGene Holdings, Inc
2650 Eisenhower Avenue
Noristown, PA 19403

EXAMINER

MCKELVEY, TERRY ALAN

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/074,744

Applicant(s)

PADIDAM, MALLA

Examiner

Terry A. McKelvey

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 1/6/04
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 11-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>6/02</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group IV, claims 1-10 in the paper filed 1/6/04 is acknowledged. The traversal is on the ground(s) that the claims of Groups I-IV are not both independent and distinct as required by the plain language of the statute which is in contradiction with the lengthy explanation in MPEP 802.01. This is not found persuasive because as described by MPEP 802.01, clearly "independent or distinct" is the intent of the statute as shown by the Court decision described in MPEP 802.01. That decision which interprets the statute is what is legally controlling regarding restriction. The applicant also argues that there would be no undue burden on the Examiner to search Groups I-IV, that they all are classified in the same class/subclass, that MPEP 803.04 states that up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction, that the search for art for a method to reduce transcription interference comprising SEQ ID NO:1 would encompass the method to reduce transcriptional interference of SEQ ID NOS:2-4 and that performing an entire search covering SEQ ID NOS:1-4 is less burdensome on the Examiner than separate

Art Unit: 1636

searches which necessarily involve duplication of searching efforts, likewise with Group V. These arguments are not persuasive because as explained in the previous communication, the undue burden comes from the four separate sequence searches (non-patent literature searches not defined by class/subclass) required in order to search the four groups. The PTO library will not search more than one independent and distinct sequence because of the burden on the sequence search system. The provisions of MPEP 802.04 are drawn to up to ten sequences will be examined; one sequence is encompassed within the up to ten. What truly governs the number of sequences to be searched is the burden. As indicated previously, it is now an undue burden in search time to search more than one sequence. The sequence search for SEQ ID NO:1 provides no information on SEQ ID NOS:2-4 because as far as the Examiner can determine, the sequences are not closely related enough so that one sequence search can be used for all four sequences. Thus, four separate sequence searches are needed to search all four groups. Regarding the argument that it is less burdensome on the Examiner to search all four Groups and sequences than separate searches, on its face, this is an unpersuasive argument because if that was true, than restriction would not be required because restriction is done in order to relieve the Examiner of undue burden in

Art Unit: 1636

examining more than one independent or distinct inventions. A requirement to do four separate sequence searches for the search of an application is clearly more burdensome than doing one sequence search because four is greater than one. This is also true for searching the claims of Group V which are classified in different class/subclasses, which is prima facie evidence of undue burden to search with the elected group.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed 1/6/04.

Claim Objections

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 2 is drawn to the positioning of the gene expression cassettes being selected from one of three possible

Art Unit: 1636

orientations. Because there are no other possible orientations, the claim does not limit the parent claim orientations to a subset of those possible and thus has the same scope as claim 1, not further limiting claim 1.


Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 4-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method to reduce transcriptional interference between two or more tandemly arranged gene expression cassettes in a host cell comprising having a spacer polynucleotide between the cassettes, which spacer polynucleotide results in a reduction of transcriptional



interference. There is no limitation on what the spacer can be, only that it functions to reduce transcriptional interference. Thus, the method claims are genus claims because the spacers are a genus of polynucleotides only defined by function.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factors present in the claims is drawn to the function of the spacer, to reduce transcriptional interference and some claims have limitations to adenine/thiamine nucleotide content, from at least 40% to at least 63%. This provides no real structural information because these quantities cover a very high percent of nucleotide sequences and thus do not place much structural limitation on the claimed genus which for polynucleotides structural information actually is some sort of sequence information. The only structural information in the specification is that four specific sequences are described by the applicant as being functional. There is no evidence that

Art Unit: 1636

these four sequences are representative of the entire vast scope of spacer polynucleotides which in the claims are only limited by function, not structure. There is no description of what structural features are in common between the four sequences which are responsible for their activity nor is there a description of any other structural features of the spacer genus which would distinguish members of the genus from polynucleotides of at least 40% to at least 63% A/T which do not act as spacers that reduce transcriptional interference. Accordingly, in the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is now is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of spacer polynucleotides that function as claimed, and therefore

Art Unit: 1636

conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation or identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the claimed methods limited to one of the four sequences set forth (but, because of the restriction, limited to SEQ ID NO:4), but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

Art Unit: 1636

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, the use of "interference between two or more tandemly arranged gene expression cassettes" renders the claims vague and indefinite because the claim only recites one spacer between two cassettes; there is no indication of more than two cassettes nor is there an indication of more than one spacer for the additional spaces between the additional cassettes.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 and 4-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Eggermont et al (Applicant reference AH).

Eggermont et al teach introduction into a host human cell two tandemly arranged gene expression cassettes, each driving the expression of a truncated human alpha2 globin gene (which reads on an antigen because it is antigenic like most proteins) (page 2541, column 1). This reference teaches that the two expression cassettes interfere with the expression of each other, which expression interference is alleviated by insertion of a poly(A) signal or a transcriptional pause site or both between the expression cassettes (abstract). Although the actual A/T content of the poly(A) signal and transcriptional pause site is not taught, claims 4-7 are drawn to the spacer polynucleotide comprising at least up to 63% A/T content, which is open language, and thus if only a part of the poly(A) signal and/or transcriptional pause site is A/T rich (which is certainly true for at least a portion of the elements), then it meets the claim limitations because the claims are open to the rest of the element being low in A/T content.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1636

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2 and 4-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ingelbrecht et al (Applicant reference AK).

Ingelbrecht et al teach introduction into a host cell a construct made by insertion of a poly(A) signal/terminator between two tandemly arranged gene expression cassettes blocks readthrough which restores the expression of the gene in (abstract; page 241, columns 1-2). The poly(A) signal/terminator reads on a spacer nucleotide because it reduces the transcriptional interference. Although the actual A/T content of the spacer is not taught, claims 4-7 are drawn to the spacer polynucleotide comprising at least up to 63% A/T content, which is open language, and thus if only a part of the poly(A) signal/terminator is A/T rich (which is certainly true for at least a portion of the element), then it meets the claim limitations because the claims are open to the rest of the element being low in A/T content. The cell taught for the method is tobacco (page 240, column 1). At least one of the gene expression cassettes is nptII, which at least reads on an

Art Unit: 1636

antigen because essentially all polypeptides are antigens. This reference teaches "Using chimeric gene constructs we demonstrate that transcriptional activity interferes with the expression of a downstream gene in opposite orientation in transient expression and is much more pronounced in transgenic plants. ... A poly(A) signal/terminator can substantially reduce readthrough from the upstream promoter, and thereby alleviate this interference."

Ingelbrecht et al do not specifically teach that the second gene expression cassettes encodes a polypeptide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to replace the nucleic acid expressed by the second gene expression cassette in the method taught by Ingelbrecht et al with a gene encoding a second desirable protein to be expressed because it is well within the ordinary skill in the art to express two genes as shown by Ingelbrecht et al for a second gene which does not encode a polypeptide and it is well within the ordinary skill in the art to replace one gene with another desirable one, such as one encoding a second desirable polypeptide.

One would have been motivated to do so for the expected benefit of making a plant expression vector that expresses two desirable proteins without interference using a poly(A)

signal/terminator as taught by Ingelbrecht et al. Based upon the teachings of the cited reference, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 703-872-9306. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning rejections or other major issues in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM

Art Unit: 1636

to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on (571) 272-0781.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

March 22, 2004